REMARKS

Claims 1-2, and 7-9 are pending, claims 3-6 and 21 having been canceled by the present amendment. Claims 1 and 2 have been amended; the amendment is supported by disclosure throughout the specification, e.g., at page 1, line 34, to page 2, line 13, and at page 4, lines 1-12, of the specification. Claim 2 has been amended to correct a typographical error.

The title and abstract have been amended as requested by the Examiner. The abstract is supported by the abstract on the cover page of the corresponding PCT application (WO 99/57248).

No new matter has been added by this amendment.

Rejections Under 35 U.S.C. § 112, first paragraph

Claims 1-9 and 21 were rejected for overbreadth and lack of enablement. Claims 3-6 and 21 were canceled.

With respect to overbreadth, the Examiner stated

> The above invention is drawn to an enriched population of mammalian neural precursor or dopaminergic neuron precursor cells said cells being characterized in that they exhibit a stem cell phenotype in the presence of a Wnt polypeptide and differentiate into dopaminergic neurons in the absence of said Wnt polypeptide. The language of said claims encompasses Wnt polypeptides including Wnt-1, Wnt-2, Wnt-3a, Wnt-7a, and Wnt-7b. (page 4, lines 3-7, of the Office Action)

Claims 1 and 2 have been amended to require a polypeptide containing the amino acid sequence of SEQ ID NO:1 (human Wnt-1). Therefore, the rejection for overbreadth should be withdrawn.

With respect to enablement, the Examiner stated

> Since the specification fails to provide any guidance for the successful isolation and enrichment of said cell population, and since resolution of the various complications in regards to the culturing and characterization of stem cells is highty unpredictable, one of skill in the art would have been unable to make the invention without engaging in undue

> trial and error experimentation. In order to practice the invention using the specification and the state of the prior art outlined below, the quantity of experimentation required to practice the invention as claimed would require de nove determination of formulations with known Wnt polypeptides and stem cell lines to correlate the presence or absence of Wnt polypeptides to the cell populations state of differentiation. In the absence of any guidance from the specification, the amount of experimentation would be undue, and one would have been unable to practice the invention over the scope claimed.

First, the scope of the claims has been amended to require a Wnt-1 polypeptide with an amino acid sequence of SEQ ID NO:1. Thus, one of skill in the art would have no trouble determining which peptide to use in cell culture. Moreover, the claims are drawn to an "enriched population". The scope of the claims is a population of cells that has been treated with a Wnt polypeptide to selectively expand a desired neural precursor cell type (see sentence spanning pages 1-2 of the specification). The claims simply require that the population "contains a higher concentration of neural precursor cells having a particular cell fate compared to the concentration in a naturally-occurring population of stem cells" (page 2, lines 4-7, of the specification). Determining the concentration of one phenotype of cell compared to another is also well within the purview of those skilled in the art of cell culture and cell differentiation.

Second, the methods required to achieve such a population are described in copious detail in the specification and are augmented by decades of cell culture methodology known in the art. In other words, culturing cells with various compositions to influence their differentiation and function is well known in the art. The significant contribution to the art provided by the inventors is which composition to use to achieve the desired effect of enriching for neuronal precursor cells. The claims have now been amended to reflect that contribution, and the disclosure provides ample guidance regarding how to obtain and culture cells in the presence of a Wnt-1 polypeptide.

The specification teaches "Neural precursor cells selectively proliferate in the presence of the Wnt polypeptide, whereas other precursor cells do not proliferate (or proliferate at a rate lower than that of the dorsal neural precursor cells)" (page 2, lines 25-29, of the specification). Determining whether cells proliferate more or less in the presence of a particular composition, in this case Wnt-1, is well within the skill of the art. Moreover, the specification teaches how to

achieve the claimed population of cells such as how to obtain the starting population (page 7, lines 30-32; page 14, line 29, to page 15, line 15, of the specification). Methods of dissociating tissue-derived cells, media formulations, feeder cells, pH consideration, are also described. Even very specific aspects of the procedure such as length of culture are disclosed in detail (page 16, lines 16-33, of the specification). The specification further reports data regarding the effect of the Wnt-1 polypeptide on cell differentiation (Example 1 of the specification).

In view of the amended scope of the claims and the guidance provided in the originally filed specification, Applicants respectfully request withdrawal of the rejection for overbreadth and enablement.

CONCLUSION

In view of the foregoing response, Applicants submit that the application is in condition for allowance and such action is respectfully requested.

A petition for extension of time and a check in the amount of $475.00 is enclosed to cover the petition fee for a three month extension of time pursuant to 37 C.F.R. § 1.17(a)(3). The Commissioner is hereby authorized to charge any fees that may be due, or credit any overpayment of same, to Deposit Account No. 50-0311, Reference No. 21508-022Natl.

Should any questions or issues arise concerning the application, the Examiner is encouraged to contact the undersigned at the telephone number provided below.

Respectfully submitted,

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